OPTOMETRY

INVITED REVIEW

Orthokeratology review and update

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Orthokeratology (OK) is a clinical technique that uses specially designed rigid contact lenses to reshape the cornea to temporarily reduce or eliminate refractive error. This article reviews the history of traditional daily-wear OK (1960s to 1980s) and discusses the reasons for the recent resurgence in interest in the new modality of overnight OK, using reverse-geometry lens designs (1990s to the present). The clinical efficacy of the current procedure is examined and outcomes from clinical studies in terms of refractive error change and unaided visual acuity are summarised. Onset of the effects of overnight OK lens wear is rapid, with most change after the first night of lens wear and stability of refractive change after seven to 10 days. Mean reductions in myopic refractive error of between 1.75 and 3.33 D and individual reductions of up to 5.00 D have been reported. There appear to be slight reductions or minimal changes in astigmatism with the use of reverse-geometry lenses and most patients are reported to achieve 6/6 unaided vision or better. The induction of higher order aberrations, in particular, spherical aberration, has been reported and this may affect subjective vision under conditions of low contrast and pupil dilation. Patient satisfaction with overnight OK has been reported as similar to or better than with other popular modalities of contact lens wear. Available evidence suggests that the corneal changes induced by overnight OK are fully reversible. The refractive effect in OK is achieved by central epithelial thinning and this has raised concerns about compromise of the epithelial barrier to microbial infection. Recent reports of microbial keratitis in the modality are reviewed and the overall safety of the procedure is examined critically. Recent research on stromal contributions to the OK effect, particularly relating to overnight oedema, is summarised. Emerging issues in OK, including myopic control, correction of other refractive errors and permanency of the OK effect, are discussed.

Orthokeratology (also called OK, ortho-k, corneal reshaping, corneal refractive therapy or CRT, and vision shaping treatment or VST) is a clinical technique that uses specially designed and fitted rigid contact lenses to reshape the corneal contour to temporarily modify or eliminate refractive error. Today, the most common clinical application of orthokeratology (OK) is for the reduction of myopia through corneal flattening, although new lens designs targeting astigmatism, hyperopia and presbyopia are under development.

OK is not a new procedure but has experienced a resurgence in clinical and research interest over the past decade. In 1971, during the heyday of 'traditional' OK, the International Orthokeratology Section of the National Eye Research Foundation defined OK as 'the reduction, modification or elimination of refractive

Exhibit 2

anomalies by the programmed application of contact lenses'. Despite significant changes in OK lens designs, materials and wearing regimens over the past 35 years, this early definition remains valid.

In this article, I review the history of OK and the reasons for the recent reawakening of interest in this modality. The clinical efficacy of modern overnight OK in terms of myopic reduction, changes in corneal topography and visual and optical outcomes will be summarised. Research investigating the mechanisms underlying the corneal response to OK will be discussed. Recent concerns about the safety of overnight OK will also be examined, particularly with reference to microbial keratitis. Finally, I will comment on the future directions of OK.

This review is not intended as a practical guide to the clinical application of OK. The interested reader is referred to the recently published book by Mountford[1] or to the many other excellent papers that describe OK lens design, approaches to OK lens fitting and management of the OK patient.[2,3]

TRADITIONAL OK. THE EARLY YEARS

Unconfirmed stories suggest that in ancient times, the Chinese slept with small weights or sandbags on their eyelids to reduce myopia: the principle is certainly similar to modern OK. More than one century ago, in the very early days of glass scleral contact lenses, the French ophthalmologist Eugene Kalt attempted to modify corneal curvature in keratoconic patients by using flat-fitting lenses that applied pressure against the cone.[4] It was not until the advent of the corneal lens that the possibility of deliberately manipulating corneal shape with contact lenses to modify refractive error began to be recognised.

Soon after the introduction of polymethyl methacrylate (PMMA) corneal contact lenses in the 1950s, practitioners began to notice unintended changes in corneal curvature and refractive error in some patients, particularly when the lenses were fitted flatter than corneal curvature. Morrison[5] reported a series of more than 1,000 young myopic patients

wearing flat-fitting PMMA lenses, none of whom showed any progression of myopia over two years. The authors attributed this, in part, to contact lens-induced corneal flattening. The changes in corneal curvature and refractive error induced by PMMA lens wear led to attempts to intentionally modify myopia through controlled corneal flattening using contact lenses.

The father of modern orthokeratology is undoubtedly George Jessen. In 1962, he delivered a lecture to the Second International Congress for Contact Lenses in Chicago, in which he first described his 'orthofocus' technique and this was followed by two papers that expanded on his methods for myopic reduction.[6,7] Unlike the more commonly used alignment lens fitting philosophy, Jessen fitted myopes with conventional plano-powered PMMA lenses that were flatter than the corneal curvature by the amount of myopia and utilised the post-lens tear fluid lens to correct the myopic refractive error. Over time, he found that the cornea flattened, allowing improved unaided vision after contact lens removal. Jessen[7] also applied this principle in hyperopic patients using steep lenses and reported some success.

Over the next two decades, the technique, renamed 'orthokeratology', was developed and refined by a number of enthusiastic practitioners, including Neilson, Grant, May, Nolan, Ziff and Tabb. At that time, so-called 'traditional' OK fitting approaches aimed to stabilise and centre the otherwise unstable lens, which tended to show poor centration due to the flat central base curve. Corneal flattening was controlled typically by progressively changing the lens base curve in small steps and modifying optic zone diameter and peripheral curves. Lenses were worn during the day, allowing a period of improved unaided vision in the afternoon and evening, and sometimes for longer periods. Treatment often took weeks to months, with variable and unpredictable outcomes. Interestingly, it was found that lenses fitted slightly steeper than corneal curvature could induce corneal flattening and reduction of myopia, while maintaining adequate centration.[8] Most reports

from this early period comprised clinical anecdotes and it was not until the late 1970s that scientific attention turned to OK.

Kerns[9] was the first to conduct a clinical investigation of the efficacy of traditional daily-wear OK, using large diameter PMMA lenses in a conventional design but fitted flatter than K. In a series of papers published between 1976 and 1978, he described a three-year study in which he compared myopic subjects wearing OK lenses, conventional PMMA lenses fitted in corneal alignment, and spectacles. Modest reductions in myopia (spherical equivalent) were found in both OK and conventional lens-wearing subjects (0.77 ± 0.91 D and 0.23 ± 0.48 D, respectively) after 300 days of lens wear. Changes in refractive error in the OK group ranged from 2.62 D decrease to 1.00 D increase in myopia. Kerns[9] also reported the induction of an average of 0.42 D with-the-rule corneal astigmatism in OK subjects, due to lens decentration and instability. He noted that the cornea tended to become more spherical (less aspheric) during OK and he was the first to postulate that corneal sphericity was the end-point of OK treatment.

Over the following five years, three other papers were published describing clinical investigations into traditional daily wear OK. In 1980, Binder reported on clinical outcomes using an OK fitting approach developed by his co-authors, the OK pioneers May and Grant.[10] As with the Kerns study,[9] the OK lenses were large diameter PMMA lenses of conventional design, fitted flatter than K. This study[10] was marred by a high drop-out rate: less than 50 per cent of the 20 subjects fitted with OK completed more than 18 months of lens wear. Overall, clinically significant but modest reductions in myopia were found at 18 months, averaging 1.51 ± 1.10 D in moderate myopes (greater than -2.50 D at baseline) but only 0.39 ± 0.99 D in lower myopes (less than -2.50 D). The control group fitted with alignment PMMA conventional lenses also showed a reduction in myopia, although this was confounded by the high drop-out rate. Overall, the authors commented that the

Authors (year)[ref]	Period of OK lens wear	OK lens wear: change in myopia (mean ± SD)	Conventional lens wear: change in myopia (mean ± SD)
Kerns (1976–1978)[9]	3 years	0.77 ± 0.91 D	0.23 ± 0.48 D
Binder et al (1980)[10]	18 months[a]	1.51 ± 1.10 D (>-2.50 D[b]) 0.39 ± 0.99 D (<-2.50 D[b]) Overall 1.24 D	Reduced myopia, but specific data not reported
Polse et al (1983)[11]	18 months	1.01 ± 0.87 D	0.54 ± 0.58 D
Coon (1984)[13]	18 months	1.30 ± 0.89 D (maximum change)	0.96 ± 0.95 D (maximum change)

[a] some subjects were followed for 33 months but there were significant drop-outs after 18 months
[b] baseline refractive error

Table 1. Summary of clinical outcomes from published studies of traditional daily wear orthokeratology (OK)

technique showed high variability and unpredictability. They also reported the induction of an average of 0.82 D corneal astigmatism in the OK wearers and noted that the refractive and visual effects of OK were not permanent, with rapid recovery to prefitting levels on cessation of lens wear.

The most important study during this early period was undoubtedly the Berkeley Orthokeratology Study reported by Polse and his colleagues[11] in 1983, because of the scientific rigour applied to their study design and the careful analysis of their data. Subjects were randomised to wear conventional or OK PMMA lenses. Forty subjects were recruited in each group, although about 25 per cent of subjects failed to complete the study. Modest reductions in myopia were found for both groups after 18 months, with significantly more change in the OK group compared with the conventional lens wearers (1.01 ± 0.87 D versus 0.54 ± 0.58 D). Regression of the refractive effect after discontinuing lens wear was also monitored for up to three months, by which time about 75 per cent of the OK effect had dissipated, clearly demonstrating that any refractive effect of OK lens wear was temporary. Polse and colleagues[12] concluded that although OK had limited clinical effect, the procedure was safe.

The final study in this series, conducted by Coon[13] from Pacific University and pub-

lished in 1984, evaluated Tabb's OK fitting technique, which used lenses fitted slightly steeper than flat K and manipulation of the optic zone diameter to achieve corneal flattening and myopic reduction. Over an 80-week period of daily wear, subjects wearing OK and conventional lenses demonstrated modest reductions in myopic refractive error, reaching a maximum of 1.30 ± 0.89 D in the OK group (range +0.25 to +5.00 D), compared with 0.96 ± 0.95 D (range -1.25 to +3.35 D) in the conventional lens wearers. Coon[13] commented that the use of a slightly steep OK lens-fitting philosophy maintained good lens centration, minimising the induction of corneal astigmatism during OK treatment.

The conclusions from these four early studies of traditional daily-wear OK were remarkably similar. Although clinically significant mean reductions in myopia were found, these were modest and not very different from the effects obtained with conventional alignment-fitted rigid lenses (Table 1). Clinical outcomes from OK were variable and unpredictable. Any refractive change was temporary and continuing wear of a 'retainer' lens was required to maintain the refractive effect. This was considered a disappointment at that time, as the goal of OK was to induce a permanent reduction in myopia. A further drawback was the induction of significant regular with-the-rule and irregular

corneal astigmatism in some patients due to lens instability and decentration. Otherwise, the technique was reported to be safe and no significant adverse events were reported.

THE REBIRTH OF OK

For the next decade after the publication of these clinical studies, OK remained a 'fringe' technique, pursued by a small number of enthusiasts but without mainstream support in the optometric profession. It was not until the mid-1990s that several events conspired to reawaken clinical interest in this modality of contact lens wear.

Traditional OK was practised using relatively unsophisticated instruments such as the keratometer to monitor the effects of lens wear on corneal curvature and shape. By the early 1990s, technological developments and reduced costs brought computerised corneal topographic mapping devices within the reach of many clinical practices. These sophisticated instruments allowed accurate screening of OK patients and assisted in lens design and fitting. They proved invaluable for visualising and quantifying lens-induced changes in corneal shape and for troubleshooting in the event of unsatisfactory outcomes. Corneal topographers are now considered an integral and necessary part of modern OK lens practice. Their appli-

cation in the management of OK patients has been covered in detail elsewhere.[1-3]

In the early days of traditional daily-wear OK, the only rigid lens material available was PMMA. Because of its impermeability to oxygen, PMMA lenses induced hypoxia in most patients even during open-eye wear and overnight lens wear was clearly precluded. In the 1980s, development of rigid gas-permeable (GP) lens materials flourished and by the end of the decade a range of rigid lens polymers with high oxygen permeability (Dk) were available on the market. These materials allowed significant transmission of oxygen to the cornea during closed-eye lens wear and were used successfully and safely for extended wear in conventional lens designs.[14] It was not long before the obvious advantages of closed-eye wear of OK lenses were recognised and overnight OK was born. In this modality, OK lenses are worn only during sleep and are removed soon after awakening. The goal of overnight OK is to provide the patient with clear unaided vision during all waking hours. Overnight lens wear must be maintained to retain the refractive effect, although some patients reportedly retain good unaided vision for up to three or more days between overnight lens-wearing occasions.

The most important development, which led directly to the recent growth in interest in OK, was undoubtedly the development of the reverse-geometry lens design. Conventional rigid lens back surface designs typically are structured as a series of progressively flattening concentric curves surrounding a central base curve fitted in alignment with the central cornea. In contrast, the reverse-geometry design for myopic OK features a central optic zone fitted flat relative to central corneal curvature, surrounded by one or more steeper secondary or 'reverse' curves. The steeper secondary reverse curve or curves allows the use of a flat central base curve by acting to stabilise and centre the lens. Assessment of the lens fitting with fluorescein reveals an annulus of corneal clearance under this reverse-curve zone (Figure 1), surrounding the central optic zone, which shows close cor-

Figure 1. Fluorescein pattern under an orthokeratology lens (BE design) viewed in white light. Fenestrations are apparent in the reverse-curve zone (photo courtesy of Edward Lum).

neal alignment or apparent light bearing. Peripheral to the reverse-curve zone is a flatter curve fitted in corneal alignment and sometimes an extra peripheral curve to provide edge lift. The peripheral alignment curve controls the overall lens fitting by supporting the weight of the lens in the periphery. Aspheric curves or tangents are often used in this zone. Many variations on this general reverse-geometry lens design are marketed around the world for OK treatment of myopia. The interested reader is referred to other excellent reviews of reverse-geometry OK lens designs and fitting procedures.[1-3]

It deserves to be acknowledged that Jessen[7] described a similar lens design concept in 1964, as a means to avoid lens decentration in his orthofocus technique:

'It would be necessary to grind a concave surface with a flatter portion in its centre and a steeper portion peripherally ... The central portion would act to flatten the corneal apex. The intermediate portion would act to centre the lens.'

Furthermore in 1972, Fontana[15] used a similar approach to stabilise the flat-fitting lens base curve in his 'one piece bifocal' OK lens design. At that time, the lens design was very difficult to fabricate and

the lenses were relatively thick and uncomfortable to wear. Despite these difficulties, Fontana reported relatively rapid reductions in myopia, within six weeks of commencing daily lens wear, in 75 of 78 myopic patients fitted with the lenses. After a series of lens changes to progressively flatten the base curve, Fontana claimed good success in eliminating up to 3.00 D of myopia.

Credit for introduction of the reverse-geometry lens design in the modern era must be shared by Richard Wlodyga and Nick Stoyan. In the early 1990s, these pioneers described a novel OK lens design that they reported to induce rapid changes in myopic refractive error, within days to weeks, without the problems associated with poor lens centration.[16,17] The development of sophisticated computer-controlled lathing methodologies at about this time allowed easy fabrication of these new relatively complex reverse-geometry lens designs. The new approach to OK using reverse-geometry lenses was dubbed 'accelerated' OK because of the speed of corneal change compared with traditional OK, where clinically significant effects could take weeks to months to achieve.

Nowadays, OK is widely used around the world for the temporary correction of low to moderate myopia, using four- or five-curve reverse-geometry lenses in high Dk materials in an overnight lens-wearing modality. Estimates of worldwide usage of overnight OK have not been published. At the 2005 Global Orthokeratology Symposium (GOS) in Chicago, Jacobson[18] reported that current usage was highest in East Asia, particularly in children and adolescents, and estimated that more than 150,000 patients were wearing this modality in the region, although many more had been fitted and discontinued. Reportedly, up to 80,000 patients have been fitted in the USA,[19] 10,000 in the Netherlands[18] and more than 3,500 in Australia.[20]

Overnight OK is reported to provide many benefits for the successful patient. Comfort and convenience are enhanced because the lenses are worn only during sleep, minimising discomfort arising from lens-lid interactions and allowing device-free clear unaided vision during waking hours. The lenses are usually large (10.6 to 11.00 mm in total diameter), further enhancing comfort. Problems associated with open-eye rigid lens wear, such as 3 and 9 o'clock staining and lens-related ocular dryness, are avoided but lens adherence associated with closed-eye lens wear is frequently reported. Concerns have been raised relating to the increased risks of overnight lens wear compared with open-eye wear, particularly in terms of microbial keratitis and this issue is discussed below.

CLINICAL EFFICACY OF OVERNIGHT OK

There is now considerable evidence from clinical studies that OK using reverse-geometry lenses is efficacious for correcting myopia up to about 4.00 D, using both daily (open-eye) wear and overnight wear modalities. Refractive and visual outcomes from published clinical studies[21-36] are summarised in Table 2. In 2000, Lui and Edwards[21] published the results of a three-month clinical study of daily wear OK using Contex design OK lenses, and reported an average reduction in myopia

of 1.50 ± 0.45 D and an average improvement in vision of 0.64 ± 0.22 logMAR (about 6.5 lines). In a paper examining corneal thickness changes in OK, Swarbrick, Wong and O'Leary[22] reported an average myopic reduction of 1.71 ± 0.59 D after one month of daily wear of Contex OK lenses. Fan and colleagues[23] reported on clinical outcomes in a mix of daily wear and overnight OK patients fitted in China. In their unselected young adolescent study population, with pretreatment refractive errors of up to 10.75 D of myopia and 3.00 D of astigmatism, the average reduction of myopia over a six-month period was reported to be 3.00 D, ranging up to 5.00 D, and astigmatism was also reduced by about two-thirds.

In 1997, Mountford[24] was the first to report the clinical outcomes of overnight OK. In a retrospective analysis of 60 cases, he found a mean reduction in myopia of 2.19 ± 0.80 D, with a maximum reduction of 5.00 D. In the first prospective study of overnight OK, published in 2000, Nichols and associates[25] fitted 10 patients with Contex OK lenses and followed them for two months; eight subjects completed the study. Myopic reduction at the end of the study averaged 1.84 ± 0.81 D, with a range from 0.50 to 3.50 D. Since then, similar outcomes have been reported from a number of retrospective and prospective clinical studies of overnight OK and other OK-related research conducted by different research groups[26-36] (Table 2). The reductions of myopia from prospective studies have been similar, with mean refractive changes of between 1.75 D and 3.33 D and with individual outcomes ranging up to about 5.00 D reduction in myopia.

The refractive outcomes reported from these clinical studies are likely to be influenced by the refractive error profile of the participating subjects. Most clinical studies appear to exclude subjects with more than about 4.00 D of myopia. No studies have directly investigated the safe upper limit of refractive change that is achievable with current lens designs used in overnight OK, although there have been anecdotal accounts of large OK-induced refractive changes exceeding 6.00 D.[37,38]

Despite the many different OK lens designs available, there is little evidence to suggest clinically significant differences in efficacy between designs. In a one-month prospective study comparing four reverse-geometry lens designs for overnight OK, Tahhan and colleagues[27] were unable to find any clinically or statistically significant differences in the refractive or visual outcomes among the four lens designs.

Reports from clinical studies of unaided vision achieved after OK treatment strongly support the conclusion that overnight OK can target a desired reduction of myopic refractive error with reasonable accuracy. In the clinical application of overnight OK, this is obviously an important consideration when evaluating the efficacy of the technique. In more recent clinical studies (summarised in Table 2), a large majority of study participants is reported to achieve unaided vision of 6/6 or better. As can be seen from inspection of Table 2, improvements in unaided vision reported in various published clinical studies appear to be consistent with the respective reported reductions in myopic refractive error.

Although there are few reports of clinical studies of overnight OK from Asia, it is apparent that higher myopic refractive errors (up to 6.00 D or more) are often treated in this region than is typical in Western countries.[29,39] This may reflect the higher incidence of myopia, and higher degrees of myopia, in East Asian countries.[40,41] Because current OK lens designs are relatively less successful in correcting myopia much above 4.00 D, this may result in unsatisfactory levels of unaided vision in higher myopes and the necessity for supplementary visual correction to achieve satisfactory vision in some cases. Despite this apparent disadvantage, reports[39] suggest that many highly myopic patients, who might be considered to be under-corrected by OK, appreciate their reduced dependence on spectacles and the thinner corrective lenses required for clear vision.

Clinical studies of overnight OK are remarkably consistent in describing other clinical features of overnight OK. The

Authors (year)[a]	Modality	No. of patients (age; mean ± SD, or range)	Lens Type	Follow-up (mths)	Initial myopia Mean ± SD (range)	Myopic reduction Mean ± SD (range)	Change in VA Mean ± SD	Final unaided vision Mean ± SD
Swarbrick et al (1998)[22]	DW	6 (21 to 27 yrs)	Contex OK	1	-2.36 ± 0.90 D (-0.75 to -3.25 D)	1.71 ± 0.59 D	—	—
Fan et al (1999)[23]	DW/ON	54 (11 to 15 yrs)	Orthofocus B, Sightform	6	(-1.25 to -10.75 D)	Mean 3.00 D, (1.25 to 5.00 D)	—	—
Lui and Edwards (2000)[21]	DW	14 (23 ± 3 yrs)	Contex OK	3	-2.12 ± 0.51 D	1.50 ± 0.45 D	-0.64 ± 0.22 logMAR	+0.20 ± 0.20 logMAR
Mountford (1997)[24]	ON	60 (28 ± 12 yrs) (12 to 68 yrs)	Contex OK	~2	-2.19 ± 0.80 D (-1.00 to -5.00 D)	2.19 ± 0.57 D (0.50 to -3.50 D)	—	—
Nichols et al (2000)[25]	ON	10 (26 ± 4 yrs) 8 completed	Contex OK	2	-1.84 ± 0.81 D (-1.00 to -3.50 D)	1.83 ± 1.23 D (to -0.02 ± 0.81 D)	-0.55 ± 0.20 logMAR	-0.03 ± 0.16 logMAR
Rah et al (2002)[26]	ON	60 31 completed	Fargo 6, Paragon CRT	3	R -2.14 ± 0.98 D L -2.16 ± 1.00 D	R 2.08 ± 1.11 D L 2.16 ± 1.05 D	—	R 74% 6/6 L 61% 6/6
Tahhan et al (2003)[27]	ON	60 (20 to 37 yrs) 46 completed	Rinehart & Reeves, BE, Dreimlens, Contex	1	R -2.24 ± 0.77 D L -2.25 ± 0.81 D (-1.00 to -4.00 D)	2.00 ± 0.34 D	7 lines	+0.02 ± 0.14 logMAR
Soni et al (2003)[28]	ON	10 (21 to 43 yrs) 8 completed	Contex OK	3	-1.76 ± 0.70 D	Mean 2.12 D	Mean -0.62 logMAR	Mean -0.13 logMAR; 100% 6/6 or better
Cho et al (2003)[29]	ON	69 (5 to 46 yrs, median 12 yrs)	Contex OK	1 to 12	-3.93 ± 2.30 D (+0.50 to -12.50 D)	—	—	90% 6/6 in either eye
Alharbi and Swarbrick (2003)[30]	ON	18 (22 to 29 yrs)	BE	3	-2.63 ± 0.68 D (-1.25 to -4.00 D)	2.63 ± 0.57 D	—	—
Joslin et al (2003)[31]	ON	9 (34 ± 10 yrs)	Paragon CRT	1	-3.33 ± 1.26 D (-2.25 to -6.00 D)	3.08 ± 0.93 D (to -0.22 ± 0.36 D)	—	-0.07 ± 0.18 logMAR
Owens et al (2004)[32]	ON	20 (17 to 37 yrs)	BE/ABE	1	-2.28 ± 0.84 D (-1.00 to -4.00 D)	Mean 2.27 D (to +0.01 ± 0.6 D)	—	—
Hiraoka et al (2004)[33]	ON	31 (10 to 44 yrs)	Emerald	12	-2.32 ± 1.18 D (-0.50 to -6.00 D)	Mean 2.16 D (to -0.16 ± 0.33 D)	>8 lines	-0.07 ± 0.10 logMAR
Maldonado-Codina et al (2005)[34]	ON	24 (28 ± 10 yrs) 9 completed	BE, No7	0.25 (7 days)	BE -2.22 ± 0.63 D No7 -2.40 ± 0.59 D	BE mean 2.89 D (to +0.67 ± 0.86 D) No7 mean 2.23 D (to -0.17 ± 0.50 D)	8 lines	BE: -0.04 ± 0.10 logMAR No7: +0.06 ± 0.15 logMAR
Sorbara et al (2005)[35]	ON	30 (28 ± 7 yrs) 23 completed	Paragon CRT	1	-3.00 ± 1.63 D	2.59 ± 0.77 D (1.25 to 3.88 D)	>9 lines	83% ≤ 6/6
Berntsen et al (2005)[36]	ON	20 (21 to 37 yrs)	Paragon CRT	1	-3.11 ± 0.96 D (-1.00 to -5.50 D)	3.33 ± 0.96 D	—	—

DW: daily lens wear
ON: overnight lens wear
VA: visual acuity
LogMAR: logarithm of the minimum angle of resolution

Table 2. Clinical outcomes from studies of efficacy of orthokeratology using reverse-geometry lenses. Data were published in various forms in the cited papers and this is reflected in the table. Data are presented variously as mean ± standard deviation (SD), range, and mean data.

greatest reduction in myopic refractive error (approximately 75 per cent) is usually achieved after the first night of OK lens wear and the endpoint of refractive change is reached after about seven to 10 nights of wear. There is slight regression of effect (about 0.25 to 0.75 D) during the day and lenses must be periodically worn overnight (from every night to every three to four nights) to retain the effect. No serious adverse events have been reported from published clinical studies, although overnight lens adherence and clinically significant corneal staining in the morning after lens removal appear to be relatively common and have caused some clinical concerns in some studies.[21,23,24–29,32,56]

It is not surprising that satisfaction with clinical outcomes of overnight OK is good among those who successfully wear the lenses. Unlike refractive surgery, if patients fail to achieve a subjectively successful outcome, they can cease lens wear and return to other corrective options, such as spectacles or conventional contact lenses. Thus, any studies of patient satisfaction with overnight OK are likely to be biased by self-selection of happy patients.

Using quality-of-life (QOL) surveys, a number of investigators has reported high levels of patient satisfaction with overnight OK.[42–45] Rah and colleagues[42] were unable to detect any difference in QOL indices, when comparing overnight OK patients with refractive surgery patients using the National Eye Institute Refractive Error Quality of Life (NEI-RQL 42) questionnaire. Using the same instrument, Ritchey, Barr and Mitchell[43] found no differences for most QOL indices between subjects wearing overnight OK and 30-day continuous wear silicone hydrogel lenses. In a recent cross-over study, Lipson, Sugar and Musch[44] reported that patients preferred overnight OK to disposable hydrogel daily lens wear by a margin of two to one, despite better visual acuity with the soft lenses. Reduced dependence on the optical correction, fewer lens-related symptoms during the day and less limitation on daily activities were cited as reasons for this preference.

TIME COURSE OF EFFECTS OF OK

The time courses of onset and regression of clinical effects of reverse-geometry lens wear have been studied from a number of perspectives. Sridharan and Swarbrick[46] investigated the rate of onset of OK lens-induced changes over the first eight hours of lens wear. Statistically significant changes in corneal curvature and unaided vision were found after just 10 minutes of open-eye lens wear and these changes progressed significantly over the following hour. For a targeted refractive change of 2.00 D, they estimated that 60 per cent of the refractive change had occurred after one hour of lens wear and 80 per cent of the effect after the first occasion of overnight lens wear. The remarkably rapid rates of onset of lens-induced corneal flattening and refractive change with reverse-geometry lenses have since been confirmed by others.[47–49]

Clinical studies agree that corneal curvature and refractive error changes continue over the first few days of overnight OK, until stability is reached after seven to 10 nights of lens wear, as illustrated in Figure 2. Higher refractive error changes typically take longer to achieve than more modest changes.[23,32] There is some evidence (see below) that subtle changes in mid-peripheral corneal shape may continue for some weeks to months with continuing overnight lens wear, although their impact on subjective vision is probably minimal.

Because lenses are not worn during waking hours in the overnight OK modality, there is an opportunity for the induced corneal changes and refractive effect to regress during the day. All clinical studies of overnight OK report a similar pattern: early in lens wear there can be clinically significant regression of refractive effect during the day but once the target refraction is reached and the refractive error change stabilises, daytime regression lessens significantly, averaging between 0.25 and 0.75 D during the day.[23,24,33,50,56] To allow for this regression, OK practitioners tend to aim for slight overcorrection of myopia (that is, pseudo-hyperopia) on lens removal in the morn-
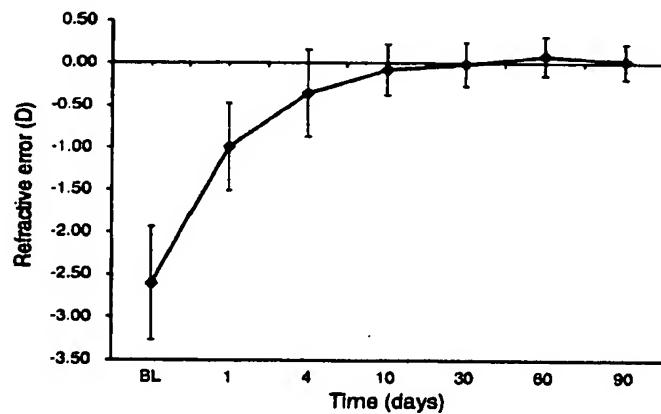

Figure 2. Changes in refractive error (spherical equivalent) with orthokeratology lenses worn overnight for three months. Data were collected in the evening, eight to 10 hours after lens removal. Error bars represent the standard deviations, BL = baseline. From Alharbi A and Swarbrick HA. The effects of overnight orthokeratology lens wear on corneal thickness. *Invest Ophthalmol Vis Sci* 2003; **44:** 2518–2523, with permission of the Association for Research in Vision and Ophthalmology.

ing, so that daytime regression does not compromise unaided vision toward the end of the day.

The rate of daytime regression tends to be greater for higher refractive corrections and earlier in OK lens wear but there are significant individual differences. Slow regression allows some patients to wear their lenses only every second or third night, or even less frequently, while maintaining adequate daytime vision. Others require nightly lens wear to avoid reduced unaided vision.

Although it is claimed that overnight OK is a reversible procedure, surprisingly few studies have directly examined this claim. Even the early studies of traditional OK did not follow their subjects to the point of complete recovery to pre-fitting values for refraction and corneal curvature. More recent studies of corneal recovery after overnight OK have been limited to relatively short OK lens-wearing periods (less than one year) and may not reflect the time course or completeness of corneal recovery after long-term overnight OK lens wear.

In an analysis of corneal and refractive recovery after six to nine months of overnight OK using the CRT lens, Barr and co-workers[51] found that 90 per cent of recovery towards baseline refractive error had occurred after 72 hours of lens wear discontinuation. On average, those who had undergone higher refractive error changes took longer to return to pre-fitting values. Similarly, Soni, Nguyan and Bonanno[52] reported rapid recovery of corneal thickness and curvature towards pre-fitting values after lens discontinuation following one month of overnight wear of the Contex OK or BE lenses. Monocular uncorrected vision had not returned completely to baseline after two weeks cessation of OK lens wear. As with other aspects of the time course of OK effects, clearly there are significant individual differences in rates of recovery. After a single overnight wearing of the BE lens, Sridharan[53] found that some subjects showed complete recovery within eight hours, whereas others took up to 72 hours for complete return to pre-fitting values for corneal curvature.

CORNEAL TOPOGRAPHIC CHANGES IN OVERNIGHT OK

The corneal topographic changes induced by reverse-geometry lenses worn for myopic OK have been well documented in a number of publications. Because of the relatively flat fitting base curve of the OK lens, a central flattened zone called the treatment zone is created, corresponding approximately to the lens back optic zone. Successful OK treatment produces a well-centred regular treatment zone that encompasses the pupil diameter, as revealed by inspection of the 'difference' map on the corneal topographer's data display (Figures 3a and 3b). The corneal topographic map induced by overnight OK is reminiscent of the corneal topographic outcome after refractive surgery (PRK and LASIK) for myopia. Indeed, this comparison is also relevant in the consideration of visual and optical outcomes of overnight OK, particularly in relation to the location and size of the treated corneal zone, as will be discussed below.
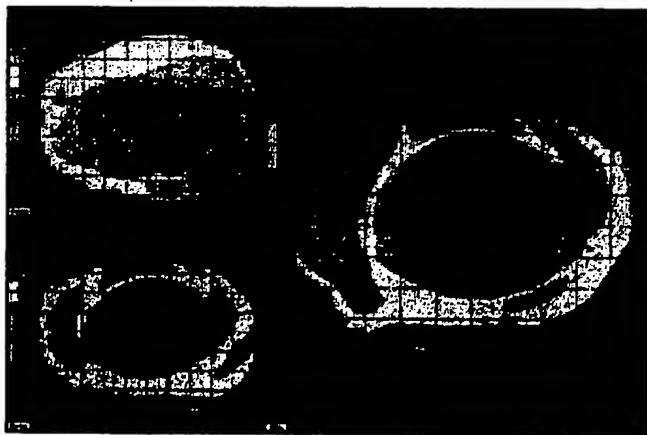
Figure 3a. Data display from the Medmont E-300 corneal topographer, showing the refractive power maps at baseline (top left), after orthokeratology treatment (bottom left) and the difference map (right) depicting a 'bull's eye' pattern following the overnight wear of an orthokeratology lens (BE design) for myopia. Figure courtesy of Edward Lum.
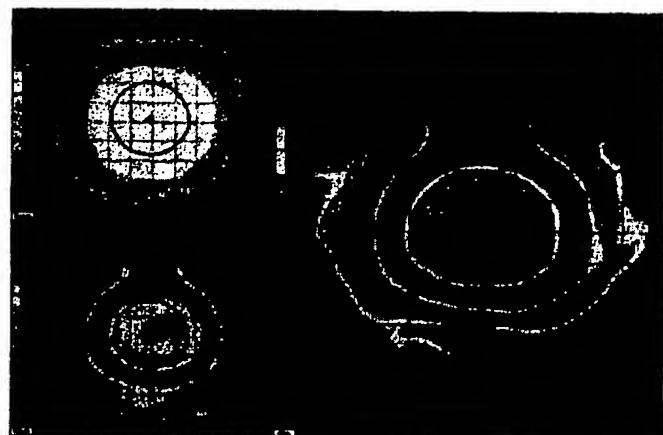

Figure 3b. Tangential power maps for the same eye. Note the mid-peripheral red ring indicating an annulus of corneal steepening. Figure courtesy of Edward Lum.

The dioptric change in apical corneal power that results from central corneal flattening in OK has been reported by Mountford[24] to correlate strongly with the change in refractive error measured by subjective refraction. Earlier studies from the days of traditional OK found that changes in corneal curvature measured by keratometry accounted for only about 75 per cent of the refractive error changes.[54,55] This inconsistency is probably due, in part, to differences between the keratometer and corneal topographer in the central corneal area measured. However, we have also found a relatively poor correlation between changes in apical corneal power and refractive error in our OK research,[55,56] suggesting that more complex changes in shape may be occurring elsewhere on the corneal surface that may also contribute to the final refractive outcome of OK lens wear.

Centration of the treatment zone in overnight OK is dependent on lens location in the closed eye and there has been little research investigating this important aspect of success in OK. In studies at our research clinic with the BE OK lenses we have noted a tendency for slight temporal lens decentration[56] and a similar trend has been reported by others using other OK lens designs.[27,57] This is likely to be related to regional topographical differences between nasal and temporal cornea and possibly also to variations in eyelid tension across the lid during eye closure. The size of the treatment zone depends on a number of variables, including lens back optic zone radius and diameter, corneal curvature and shape and the targeted refractive error change. Although this has not been specifically studied, anecdotal reports point to a reduced treatment zone diameter, when higher refractive error changes are achieved. Clearly, the size and centration of the treatment zone will influence the subjective visual outcomes of overnight OK, in much the same way as these variables can influence visual satisfaction following refractive surgery.

The central treatment zone is surrounded by an annulus of corneal steepening in the mid-periphery (as shown by the mid-peripheral red ring in Figure 3b).

This concentric zone of corneal steepening appears to coincide with the ring of corneal clearance seen in the fluorescein pattern, under the edge of the optic zone and the reverse-curve zone of the reverse-geometry lens (Figure 1). The contribution of this mid-peripheral zone of increased corneal power to the overall refractive and visual effect of OK is unclear and is likely to be pupil-dependent. Lu and colleagues[58] have argued that this zone should be considered as part of the effective refractive treatment zone in myopic OK. Alharbi[56] also found a better concordance between predicted and measured refractive outcomes of OK when this mid-peripheral zone was included in his considerations. As will be discussed below, this steepened zone probably contributes significantly to the increase in spherical aberration reported in overnight OK.

Corneal topographic changes reported in the more peripheral cornea under the alignment curve of the reverse-geometry lens are variable, including slight steepening, flattening or no change. Apparent topographic changes in this region are likely to reflect the fitting characteristics of the alignment curve of the lens relative to the mid-peripheral corneal contour and given the regional variability in corneal shape around the corneal periphery, it is not surprising that some local topographic changes are induced by the lens. Alternatively, some changes in this region may be an artefact of the algorithms used by corneal topographers to calculate difference maps, particularly if the sagittal height of the corneal apex has been displaced significantly by corneal flattening relative to the corneal periphery.

Since the early days of traditional OK, it has been noted that lens-induced central corneal flattening and mid-peripheral steepening together result in a change in overall corneal shape from the normal prolate (flattening) asphere towards a more spherical shape, where central and peripheral corneal curvatures, as measured by keratometry, correspond. This has been cited as evidence of sphericalisation of corneal shape during OK lens wear and from this has grown the clinical axiom

that the end-point of OK treatment is reached when the cornea achieves an overall spherical shape. This principle has been used for patient selection in OK and for predicting the potential refractive change achievable based on pre-fitting corneal shape. For example, Mountford[24] has proposed that potential refractive change (ΔRx; D) can be estimated from baseline corneal eccentricity (e) using the formula ΔRx = e/0.21.

Although these concepts have provided useful clinical rules-of-thumb, it is clear that corneal shape changes in OK are more complex than can be explained by changes in a single global corneal shape index.[59] Even in the normal cornea, corneal shape varies by meridian (steep versus flat) and hemi-meridian (nasal versus temporal). The corneal shape index derived by corneal topographers also depends on the chord or corneal area over which the shape index is calculated. Considerations of the unusual corneal shape changes induced by OK (and refractive surgery) are further complicated by the mathematical limitation that the most commonly used corneal shape index e (eccentricity) cannot be used to describe oblate (steepening asphere) corneal shapes. Alternative shape indices p (shape factor, $p = 1 - e^2$) and Q (asphericity, $Q = -e^2$) have been proposed to avoid this limitation[50] and are being increasingly adopted by corneal topographer manufacturers to allow the quantification of oblate corneal shapes in OK and refractive surgery.

An insight into the variations in corneal shape across the cornea during overnight OK lens wear is provided by an (unpublished) retrospective analysis of Alharbi's data[56] conducted by Kulkarni.[60] Corneal sagittal height relative to a sphere coincident with the corneal apex was calculated at 0.5 mm chord steps along the horizontal meridian of selected topographic maps and these data were used to describe corneal shape changes over three months of overnight OK. As shown in Figure 4, despite significant apical corneal flattening, there was little change in corneal shape over the central three millimetres of the cornea and this region remained rela-
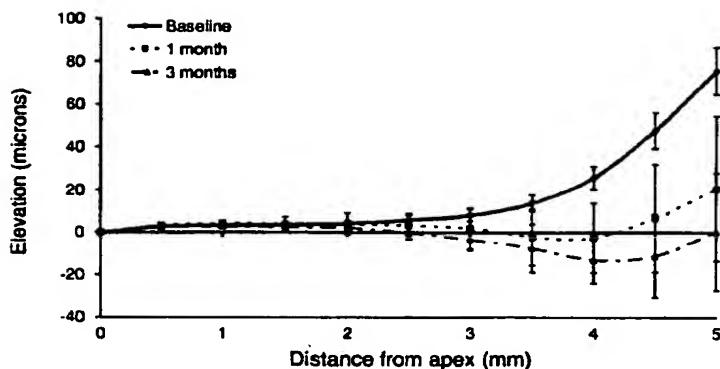
Figure 4. Elevation (in microns) of the corneal surface relative to a reference circle, with a radius equal to the apical corneal radius of curvature and coincident with the corneal apex, before and after one and three months of overnight orthokeratology lens wear. The horizontal axis (y = 0) represents a spherical shape, positive values indicate a prolate shape, and negative values an oblate shape. Data are presented for the horizontal meridian (mean of nasal and temporal hemi-meridians) for five subjects (eight eyes), based on selected Medmont E-300 topographical maps. Error bars represent the standard deviations. Data courtesy of Pancham Kulkarni.

tively spherical. Beyond the central treatment zone, corneal shape changed from markedly prolate (data points above the x-axis) before OK lens wear towards oblate (data points below the axis) after one and three months of lens wear. Interestingly, peripheral changes in corneal shape showed progression between one and three months of lens wear. This figure clearly reveals the critical dependence of corneal shape indices on the corneal area considered in the calculation; the corneal shape after one and three months of OK would be described as spherical or slightly prolate, if calculated over chord diameters up to five millimetres but oblate for longer chord lengths.

Little has been published specifically investigating differential changes in corneal topography and shape in horizontal versus vertical corneal meridians in reverse-geometry OK lens wear, and this remains an area for further study. Differential changes in corneal curvature in the two meridians would be reflected in changes in refractive astigmatism. Because the two corneal meridians usually start with different curvatures and shapes and thus, with different relationships to the OK lens base curve, it might be anticipated that the effects on corneal topography would differ between the two meridians. It should be noted that during overnight OK, the potential differential meridional effects of blinking are minimised. Clinical studies suggest that refractive astigmatism either shows no significant change,[28–28,54,56,61] or that there may be a reduction of up to 50 per cent in with-the-rule astigmatism in overnight OK.[73,62] Such a reduction in refractive astigmatism implies differential effects of OK lenses on the two meridians.

VISUAL AND OPTICAL OUTCOMES OF OVERNIGHT OK

As discussed earlier, outcomes in terms of unaided vision reported from clinical stud-

ies of overnight OK have been good, with a large majority of subjects in recent studies achieving 6/6 or better (Table 2). In clinical practice potential visual problems may arise due to under- or over-correction of myopia or significant residual refractive astigmatism. As with refractive surgery, visual disturbances may arise from a small or decentred central treatment zone, resulting in symptoms of ghosting and flare and reduced contrast sensitivity, particularly with a dilated pupil under low illumination conditions. Because of the reversible nature of OK-induced effects, unsatisfactory visual outcomes can often be corrected by modification of lens design or fitting after a short non-lens-wearing period to eliminate the unwanted corneal topographic changes.

Except in patients experiencing significant adverse events, reductions in best corrected visual acuity (BCVA) following OK treatment have rarely been reported. In their comparison of reverse-geometry lens designs for overnight OK, Tahhan[27] reported no reductions in BCVA for any lens design. Hiraoka and co-workers[63] reported a significant increase in corneal asymmetry indices and irregular corneal astigmatism in a group of 39 patients wearing overnight OK. Despite concerns about the induction of corneal irregularities with overnight OK, the irregularities reported in Hiraoka's study apparently had little effect on visual outcomes because all subjects achieved at least 6/6 unaided vision.

Several authors have now reported on the induction of higher order aberrations with the use of reverse-geometry lenses for overnight OK.[31,39,64] Reported increases in 'off-axis' aberrations, such as coma, may be explained by decentration and tilt of the central treatment zone relative to the visual axis. Of more interest is the significant increase in spherical aberration, which is largely created by the annular zone of mid-peripheral corneal steepening induced by the reverse-geometry lens, and the consequent change in corneal shape from prolate towards oblate asphericity. Joslin and co-workers[31] have reported an increase of approximately five-times in spherical aberration for a six-millimetre pupil after one month of over-

night OK lens wear and similar increases have been reported for other reverse-geometry lens designs.[36,63] According to Berntsen, Barr and Mitchell,[31] spherical aberration induced by overnight OK can reduce low contrast visual acuity by up to two lines relative to high contrast acuity under conditions of low illumination and pupil dilation.

In the same way as algorithms for laser refractive surgery have evolved in the quest for 'super vision', it is conceivable that refinements in OK lens design and fabrication and in the analysis of corneal topography and ocular aberrations, may lead to 'aberration-controlled' corneal reshaping procedures in the future.

MECHANISMS OF CORNEAL SHAPE CHANGE IN OK

In the early days of OK, it was assumed that the cornea was moulded toward the back surface shape of the contact lens as a result of pressure exerted by the lens on the corneal apex, mediated by the eyelid during blinking. This concept was certainly the basis for Jessen's orthofocus technique, in which lenses were fitted flatter than corneal curvature by the dioptric amount of the myopic refractive error. The goal of this fitting approach was to select the lens base curve to match the desired curvature of the reshaped cornea. Despite advances in our understanding of the forces governing rigid lenses on the eye,[65,66] this idea of the 'Jessen factor' has persisted and is still used today in many reverse-geometry fitting philosophies to select the OK lens base curve.[1-3]

The realisation that steep fitting lenses could also flatten corneal curvature[8] triggered a different line of thinking in some quarters. Tabb (cited by Coon[67]) developed the 'hydraulic' theory of OK, in which he argued that fluid forces in the post-lens tear film were responsible for inducing the corneal shape change. This theory was extended by Mountford and Noack[68] in their development of the BE OK lens design. Their 'ideal tear layer thickness (TLT)' fitting philosophy is based on the concept of individualising the post-lens tear film profile and thus the

tear film forces, based on the patient's corneal shape and desired refractive correction, to achieve the required corneal shape change.

Although no investigations were conducted, it was generally assumed that the corneal tissue response to traditional OK involved an overall bending and consequent flattening of the cornea. Difficulties in resolving refractive error changes with changes in keratometric readings of corneal power induced by traditional OK suggested that other changes may also be occurring elsewhere in the eye[51-56] and studies investigating changes in corneal thickness, axial length and crystalline lens power were mooted.[56] Polse and colleagues[19] found no changes in corneal thickness in their study, whereas Coon[13] reported up to 20 microns of central corneal thinning in his study with some unspecified mid-peripheral thickening. The corneal response to OK at a cellular level remained a mystery.

Swarbrick, Wong and O'Leary[22] were the first to suggest that corneal bending was not involved in the response to OK. In a one-month study of daily-wear OK with reverse-geometry lenses, they reported

central corneal epithelial thinning and mid-peripheral corneal thickening, possibly of epithelial and stromal origin. Based on a model developed from Munnerlyn's formula for PRK ablation depth,[69] they were able to demonstrate that these topographical changes in corneal thickness and the associated change in corneal sagittal height were sufficient to explain the refractive effects of OK, without the need to postulate corneal bending. Central epithelial thinning has since been confirmed in clinical studies of overnight OK,[24,26,30,70] as shown in Figure 5, and in animal models.[71,72] The nature of the mid-peripheral corneal thickening, located in an annulus under the reverse curve of the lens, is less certain. Alharbi and Swarbrick,[30] using optical pachometry in human subjects, reported that this thickening was primarily stromal in origin, whereas histological studies in the cat have suggested both epithelial and stromal components.[73] Interestingly, Nichols and associates,[25] using the Orbscan, and Haque and co-workers,[70] using optical coherence tomography (OCT), did not find any mid-peripheral corneal thickening.

The nature of the central epithelial
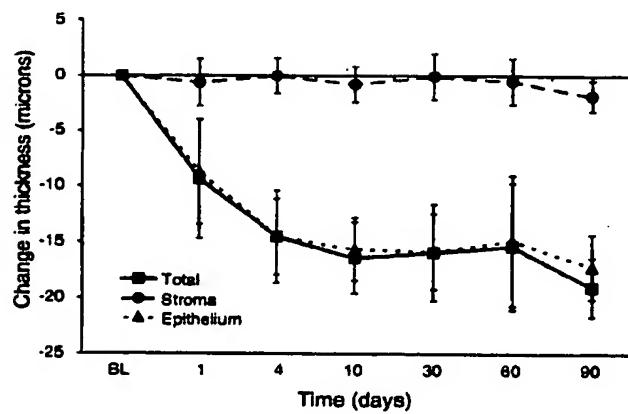
Figure 5. Changes in central total, stromal and epithelial corneal thickness induced by orthokeratology lenses worn overnight for three months. Data were collected in the evening, eight to 10 hours after lens removal. Error bars represent the standard deviations, BL = baseline. From Alharbi A and Swarbrick HA. The effects of overnight orthokeratology lens wear on corneal thickness. *Invest Ophthalmol Vis Sci* 2003; 44: 2518–2523, with permission of the Association for Research in Vision and Ophthalmology.

thinning in OK is unclear. Initially, it was postulated that this represented cellular movement away from the region of lens-induced central pressure.[22] This theory was based on earlier work by Holden, Sweeney and Collin[74] in the cat model, in which adherent silicone elastomer lenses induced heaping of the epithelial cells outside the edge of the lens. This was interpreted by Holden, Sweeney and Collin as indicating epithelial cell movement away from the pressure induced by the bound lens edge. In the case of reverse-geometry OK lens wear, it is difficult to reconcile this interpretation with the rapid onset of effect (within minutes) reported by Sridharan and Swarbrick[16] and others.

Histological evidence from the work of Choo and colleagues[71] in the cat model indicates that, within the typical time frame for OK lens wear (up to eight hours in the closed eye), the primary epithelial response in the central cornea is cell compression rather than cell movement or loss of cell layers. In particular, the basal cells became squat and rounded compared to the normal elongated shape. These changes are similar to the mid-peripheral epithelial cell changes seen in rabbits wearing steep PMMA lenses, as reported in 1973 by Greenberg and Hill.[75] Using a battery of histochemical tests, Matsubara and associates[72] have demonstrated minimal effects on epithelial cell function in the thinned central zone under OK lenses in the rabbit model. Shin and co-workers[76] have reported changes in epithelial cell proliferation rates in rabbits wearing OK lenses, with a greater increase in the central cornea than found with conventional rigid lenses. The relevance of these short-term animal studies to the clinical application of OK in human patients is unclear and further work is needed to examine longer-term effects of OK lens wear, particularly in the closed eye, on epithelial health and integrity.

The nature of the mid-peripheral corneal thickening reported by Swarbrick, Wong and O'Leary[22] in daily wear OK and by Alharbi and Swarbrick[30] in overnight OK is also unclear. Choo and colleagues[71,73] have demonstrated that, in

the cat model, this thickening has both epithelial and stromal components. The presence of a thickened epithelium with an increased number of cell layers in the mid-periphery could represent cellular movement away from lens-induced pressure as postulated by Holden, Sweeney and Collin.[74] possibly from both the central and peripheral cornea. This dramatic increase in mid-peripheral epithelial cell layers was clearly apparent in the cat only after 14 days of continuous closed-eye OK lens wear.[71] It could be argued that this represents an excessive physiological challenge that may not be directly relevant to the clinical situation in overnight OK.

Alharbi and Swarbrick,[30] who used optical pachometry in their clinical study, reported that the subtle mid-peripheral corneal thickening (averaging 10 microns) was primarily stromal in origin. Significant mid-peripheral stromal thickening was also found in the histological study of Choo and colleagues[73] after 14

continuous days of OK lens wear. The nature of this stromal change is obscure. Because the thickening was apparent in Alharbi and Swarbrick's clinical study[30] at the end of the day, after eight to 10 hours of no lens wear, it seems unlikely that this represents residual stromal oedema. In contrast, Alharbi, LaHood and Swarbrick[74] have reported an unusual profile of overnight oedema in OK lens wear, with apparent suppression or inhibition of the central hypoxic stromal oedema response (Figure 6). This apparent inhibition of central stromal oedema, with a normal oedema response in the mid-periphery, has also been reported by Wang and associates[78] using the OCT and a different OK lens design. There are several possible explanations for this unexpected phenomenon, including reduced lactate production by the thinned central epithelium under hypoxic challenge. 'clamping' of the central cornea by lens-induced pressure and the induction of lateral movement of lactate and/or water in
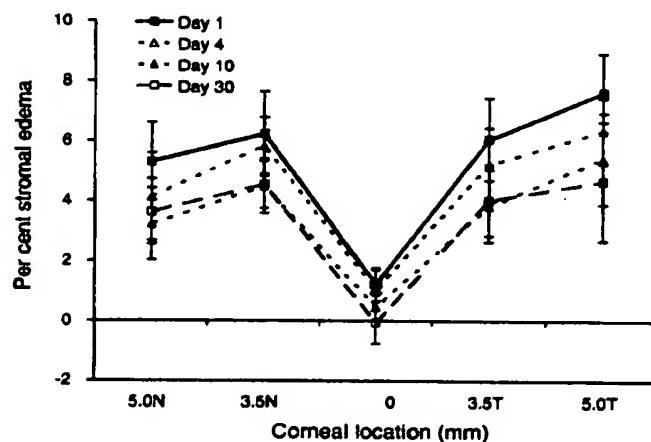

Figure 6. Overnight stromal oedema (%) across the horizontal corneal meridian in the right eyes of subjects wearing reverse-geometry orthokeratology lenses, over a one-month period. Measurements were obtained within one hour of eye opening and five minutes of lens removal. Error bars represent the standard deviations, N = nasal, T = temporal. From Alharbi A et al. Overnight orthokeratology lens wear can inhibit the central stromal edema response. *Invest Ophthalmol Vis Sci* 2005; 46: 2334-2340, with permission of the Association for Research in Vision and Ophthalmology.

the stroma under the influence of the OK lens-induced pressure profile. Further, it can be hypothesised that this unusual pattern of overnight oedema may provide an explanation for the slow and subtle changes in mid-peripheral stromal thickness during OK lens wear.

Further evidence of the contribution of the stroma to the effects of overnight OK comes from recent studies investigating the interaction between lens oxygen transmissibility (Dk/t) and clinical outcomes of OK. We conducted a masked, randomised study in which OK lenses of the same design and fitting but different Dk materials were worn during sleep in the two eyes.[79] On eye opening, there was significantly less corneal oedema in the eye wearing the moderate Dk/t lens compared with the fellow eye wearing the low Dk/t lens, as was expected. More interestingly, although OK lens-induced changes in corneal curvature and unaided vision were found as anticipated with the moderate Dk/t lenses, no clinically significant effects of OK lens wear were found in the eyes that wore low Dk/t lenses. In more recent work (by Lum E and Swarbrick H, unpublished) we have also demonstrated a reduced clinical effect with low versus moderate Dk/t OK lenses worn over a two-week period of overnight OK. These findings indicate that the stroma plays a role in the corneal tissue response to overnight OK and support the recommendation that high Dk lens materials should be used in overnight OK, not only to promote corneal health but also to optimise clinical outcomes.

Using a formula published by Munnerlyn, Koons and Marshall[70] to guide ablation depth in PRK, Alharbi and Swarbrick[30] have suggested that the topographic changes in corneal thickness can explain the refractive changes induced by OK. The formula can be expressed as:

$$t = -S^2 \cdot D/8(n-1)$$

where t is the ablation depth and S is the ablation diameter in PRK (both in metres) and D is the desired refractive change in dioptres. A refractive index n for the cornea of 1.377 is usually assumed. It should

be noted that Munnerlyn's formula assumes that the posterior cornea does not change in curvature. To apply this formula to OK data, t was taken as the change in corneal sagittal height due to the corneal thickness changes. S was taken as the OK treatment zone diameter, and the equation was solved to give D, the refractive error change predicted on the basis of corneal thickness changes alone.

Figure 7 shows the strong correlation between measured changes in refractive error and the refractive changes predicted by Munnerlyn's formula based on measured corneal thickness changes (including central thinning and mid-peripheral thickening) on day 90 at the evening measurement session. Because Munnerlyn's formula assumes that the back surface of the cornea does not change, the strong relationship between measured and predicted refractive change strongly supports the argument that corneal bending is insignificant in overnight OK.

In contrast, there is some evidence to suggest that some corneal bending may

occur, at least in the early stages of OK lens wear. Owens and co-workers[32] used Purkinje images to examine changes in posterior corneal curvature during one month of overnight OK lens wear. They found a slight but statistically significant flattening of the posterior corneal surface during the first week, which then returned towards baseline. The authors acknowledged that the effects of lens-induced overnight oedema may have played a confounding role in this interpretation of their results.

Joslin and colleagues[80] also suggested that there may be 'internal' ocular changes in addition to the obvious effects of OK lens wear on anterior corneal curvature. Their analysis of the higher order aberrations induced by OK lens wear indicated that the overall increase in aberrations could not be explained by anterior corneal changes alone. They postulated that OK lens wear may also affect posterior corneal curvature and possibly other intraocular optical structures.

There is little evidence of central
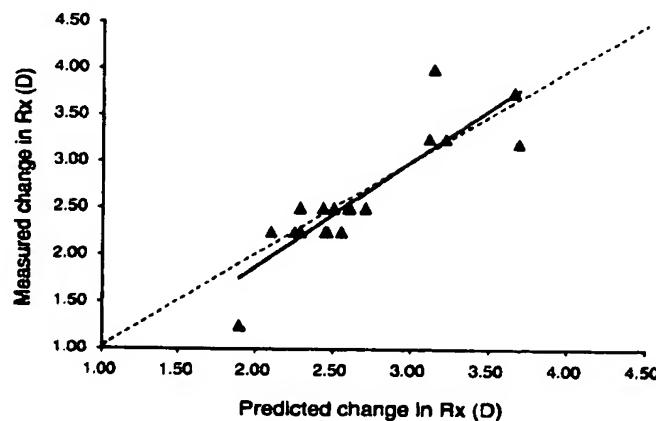
Figure 7. Relationship between refractive error changes predicted by Munnerlyn's formula, based on corneal sagittal height changes and treatment zone diameter, and refractive error changes measured after three months of overnight orthokeratology lens wear. The 1 : 1 line is shown for reference. The regression equation is $y = 1.24x + 0.37$ ($R = 0.88$; $p < 0.001$). From Alharbi A and Swarbrick HA. The effects of overnight orthokeratology lens wear on corneal thickness. *Invest Ophthalmol Vis Sci* 2003; 44: 2518–2523, with permission of the Association for Research in Vision and Ophthalmology.

corneal stromal or endothelial cellular changes accompanying overnight OK. Using confocal microscopy, Perez-Gomez and associates[81] found some slight variations in the density of anterior stromal keratocytes in the central cornea over the first week of overnight OK. Conversely, Alharbi[56] was unable to detect any change in keratocyte density in either anterior or posterior stroma over three months of OK lens wear. Similarly, he found no change in central endothelial cell density, confirming a recent report by Hiraoka and coworkers[33] of no change in endothelial cell parameters over a one-year study of overnight OK.

SAFETY OF OVERNIGHT OK

Despite the use of oxygen-impermeable PMMA lenses in traditional OK and the prolonged periods of open-eye wear of flat-fitting lenses, the technique was reported to be safe. To my knowledge, there is only one report[82] of a serious adverse event, presumed to be microbial keratitis, with traditional daily-wear OK. Binder, May and Grant[10] and Polse and colleagues[12] specifically commented on the safety of the procedure.

With the advent of overnight OK and increased understanding of the corneal changes induced by OK lens wear, there has been a growing concern about the risks that may be associated with this lens modality. It is well-established from many studies of conventionally-fitted contact lenses that overnight wear increases the risk of microbial keratitis compared with daily (open-eye) lens wear.[83–85] At the same time, it should be acknowledged that in essence, the overnight lens-wearing modalities (that is, extended wear) considered in such studies comprise continuous night and day lens wear, without lens removal for many days. This is markedly different from the lens-wearing pattern in overnight OK, in which lenses are not worn during waking hours. It might be expected that such a wearing pattern could ameliorate the effects of overnight lens wear compared with an extended or continuous lens wear regimen. The ways in which the differing patterns of lens care

(frequency, timing, risks of lens contamination) in these different lens-wearing modalities may modulate this risk is also worthy of further study.

Reverse-geometry OK lens wear induces significant (approximately 30 per cent) central epithelial thinning.[30] It is still unknown whether this thinning compromises the epithelial barrier against microbial infection. Ladage and associates[86] reported increased adherence of Pseudomonas aeruginosa bacteria to rabbit epithelium following 24 hours of continuous closed-eye wear of reverse-geometry lenses. It is not clear whether the lenses were fitted to the rabbit cornea in a fashion analogous to fitting human OK lenses. The authors presented no evidence that an OK effect had been induced nor did they inspect the rabbit corneas for epithelial staining or damage that might have been induced by inappropriately fitted lenses. Research is currently underway to clarify this important issue.

Regardless of the mechanisms underlying corneal infection in overnight OK, it is undeniable that since 2001 there has been a disturbing number of published reports of severe cases of microbial keratitis in patients wearing overnight OK lenses. Watt and Swarbrick[87] have summarised and reviewed the first 50 reports of microbial keratitis in overnight OK and further cases have since been reported in the journal *Cornea* and elsewhere. Clearly, this is cause for great concern.

The analysis by Watt and Swarbrick[87] revealed some startling trends. Over 60 per cent of affected OK patients in their series were 15 years of age and younger: four children aged nine years were affected. The majority of these early reports of microbial keratitis originated in the East Asian region, particularly in China, Taiwan and Hong Kong. Since these reports emerged, these countries have actively intervened to regulate the practice of OK.[88] Furthermore, almost 90 per cent of affected patients were of Asian ethnicity.

This demographic profile of microbial keratitis in overnight OK raises several intriguing questions. Are children more at risk of contact lens-related microbial

keratitis? There appears to have been little research in this area. Are Asian patients more at risk of contact lens-related microbial keratitis? The evidence is sparse. Certainly, the incidence of microbial keratitis associated with conventional contact lens wear appears to be only marginally higher in Hong Kong than in Europe and North America.[89] In contrast, Lin and coworkers[90] noted that Asian subjects tended to show a greater increase in epithelial permeability following overnight contact lens wear compared with Caucasian subjects, which might suggest a more easily compromised epithelial barrier in Asians. Further research appears warranted to explore these issues.

An alternative explanation for the unexpected demographic profile of microbial keratitis in OK reported by Watt and Swarbrick[87] is that this reflects the demographic profile of the worldwide OK lens-wearing population. It is undoubtedly true that overnight OK has become widespread and popular in East Asia.[14] This is probably a result of the high and increasing prevalence of myopia in the region[10,41] and the anxiety of parents searching for ways to limit or halt progressive myopia in their children. The complete range of potential 'myopic control' techniques is advocated and used in the region, including daily atropine drops, bifocal spectacles and conventional rigid contact lens wear. It is in this climate that overnight OK has flourished, built on a promise of control of myopia that has yet to be scientifically proven, despite anecdotal clinical reports.

Another feature of the analysis by Watt and Swarbrick[87] was the surprisingly high frequency of Acanthamoeba corneal infections (30 per cent of cases in their sample compared with three to five per cent in surveys of soft lens-related microbial keratitis).[91–93] Exposure to contaminated tap water is implicated strongly in Acanthamoeba keratitis and this has led to the recent recommendation that tap water should not be used in the care of overnight OK lenses or lens cases.[7,94] This has also turned the spotlight on issues of patient compliance, lens case storage and care, and the safety and efficacy of lens care solutions for this modality.[95] The con-

cern centres on the potential for placing a contaminated lens on the eye shortly before eye closure and then wearing the lens overnight in a closed-eye environment that is conducive to microbial proliferation.[96] Research in this area is necessary to ensure that appropriate lens care strategies are recommended to OK patients.

Despite the obvious emotions raised by reports of blinding disease in children wearing overnight OK,[97] some perspective should be maintained. Many of the early reports of microbial keratitis in OK, particularly from East Asia, arose during a relatively unregulated phase of growth in overnight OK, which was often practised in variable professional circumstances by practitioners untrained in fitting reverse-geometry rigid contact lenses, using lenses of uncertain provenance.[3] It is my understanding that in several Asian countries including China, Hong Kong, Taiwan and Japan, restrictions on OK practice have since been introduced, either by the government or by local professional groups, to encourage the safe practice of overnight OK, through practitioner training and certification. Hopefully this will significantly reduce the frequency of cases of microbial keratitis in overnight OK reported from these countries.

It should also be recognised that a series of case reports, no matter how shocking, does not help in determining the absolute incidence of microbial keratitis in overnight OK or the relative risk compared with other contact lens modalities. This is because reliable estimates of the number of past and current overnight OK lens wearers around the world, or even in individual countries, are difficult to obtain, and because the relatively severe cases reported in the literature probably represent the tip of the iceberg, potentially leading to an underestimation of the total number of cases of microbial keratitis in overnight OK. Therefore at this stage, it is premature to comment on the relative risk of microbial keratitis in overnight OK compared with other contact lens-wearing modalities. Studies to establish the relative risk of microbial keratitis in overnight OK and to understand the particular risk factors in this modality are clearly warranted.

Active efforts are underway internationally to clarify this issue.

EMERGING ISSUES IN OVERNIGHT OK

Control of myopia

The extraordinary growth of overnight OK in the East Asian region since the late 1990s has been driven primarily by the possibility that OK lens wear may provide not only temporary reduction but also control of myopia by inhibiting the progression of myopia during adolescence. It has been estimated that 80 per cent of overnight OK lens wearers in East Asia are 18 years of age or younger and are wearing overnight OK specifically to reduce myopic progression.[18] These figures are surprising because the published evidence supporting myopic control with OK lenses is modest and open to challenge.[98–100]

In 2004, Cho, Cheung and Edwards[100] published the results of a pilot study investigating the efficacy of overnight OK for myopic control. The study suffered from a number of scientific flaws, which were acknowledged by the authors. The study was not randomised or rigorously controlled and an historical control group of spectacle wearers was used. Furthermore, the researchers had no control over OK lens design and fitting, which was performed by independent OK practitioners. Nevertheless the results were dramatic. After six months, the OK lens-wearing subjects already showed significantly less increase in axial length and vitreous chamber depth (which are reliable correlates for myopic progression) compared to the control group and this effect was consistent throughout the two-year study period. The results of this pilot study argue strongly for a more rigorously controlled, prospective, randomised and masked clinical study to confirm these promising findings.

The possible mode of action of OK in reducing myopic progression is speculative. It has been postulated that manipulation of the visual experience of peripheral regions of the visual field through control of aberrations may influence the development of refractive error in animal models and in humans. Hypotheses such as these are being investigated around the world in a search for a cure for myopia.

If the promise of efficacious control of myopia with OK lenses is demonstrated in appropriately designed and executed clinical trials, there is no doubt that OK will flourish as a clinical modality of contact lens wear. However, until the scientific evidence is available, prudence is advised in counselling potential OK patients. An international advisory panel on corneal reshaping has recently recommended a statement of patient advice on OK and myopic control.[94]

OK for other refractive errors

Despite intense clinical interest and international research activity, reports on clinical outcomes of OK aimed at correction of other refractive errors such as astigmatism, hyperopia and presbyopia have yet to be published in the peer-reviewed literature. As with conventional rigid lenses, spherical reverse-geometry lenses can be used on toric corneas and have been reported to reduce corneal and refractive astigmatism. In a retrospective analysis, Mountford and Pesudovs[62] demonstrated that up to 50 per cent of corneal astigmatism could be reduced with standard reverse-geometry OK lenses, provided the toricity was with-the-rule and restricted to the central region of the cornea. Corneal toricity reaching from limbus to limbus on the topographic map was less amenable to modification by OK lenses. In contrast, many clinical studies report no significant mean changes in corneal or refractive astigmatism with overnight OK using reverse-geometry lenses.[26–29,35,46,61]

In Switzerland, Wyss[101] and Baertschi[102] have developed toric reverse-geometry lens designs for targeted astigmatic correction and others are working on this application of OK. These designs feature different base curve radii along the two meridians of the oval optic zone, which induce differential corneal flattening and myopic reduction in the two meridians. Early conference reports of clinical outcomes with these relatively complex lens designs are promising,[101,102] although
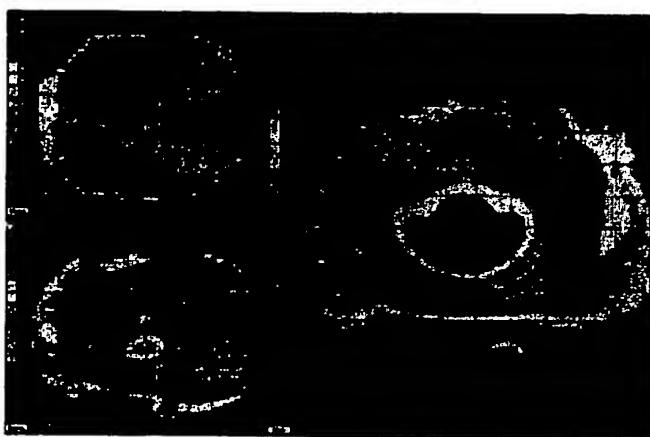
Figure 8. Refractive power maps (Medmont E-300) recorded on lens removal after overnight wear of an orthokeratology lens designed to correct hyperopia. Figure courtesy of Paul Gifford.

formal clinical studies have yet to be published.

The other frontier of OK is the development of lens designs for the targeted correction of hyperopia (and possibly presbyopia) through controlled central corneal steepening. Such a corneal shape change is possible; Swarbrick and associates[103] demonstrated slight but statistically significant corneal steepening after four hours open-eye wear of conventional apical clearance lenses. Clinical studies presented at conferences, using modifications of reverse-geometry lens designs fitted with apical clearance, have reported relatively short-term, modest, refractive effects and have not been especially encouraging.[104,105] It is apparent that corneal steepening responses may be slower in onset[106] and more variable and unpredictable than corneal flattening responses with myopic OK.

Short-term changes in corneal topography analogous to those induced by myopic OK have been described for OK lenses designed for the correction of hyperopia and astigmatism. Lenses used for hyper-

opic refractive correction induce central corneal steepening surrounded by a mid-peripheral annulus of corneal flattening in the region where the steep back optic zone of the lens approaches the cornea (Figure 8). Toric OK lenses create an oval treatment zone and different meridional topographic changes, with more corneal flattening in the meridian requiring more myopic refractive error correction. Details of corneal topographic changes induced by these different OK lens designs over longer periods of wear are yet to be published. There will certainly be further developments in these applications of OK and peer-reviewed papers reporting clinical outcomes of hyperopic and astigmatic OK over longer periods of wear are awaited with interest.

Understanding and minimising risks of microbial keratitis

The future of overnight OK is overshadowed by the spectre of microbial keratitis. It is important that this issue is addressed promptly and appropriately by the clinical and research communities. Studies to

establish the relative risk of microbial keratitis in overnight OK compared with other lens-wearing modalities, and to understand the particular risk factors in this modality, are clearly warranted. The investigation and development of clinical strategies to minimise risks of microbial infection during overnight OK are also indicated.

Overnight lens wear is well recognised as a risk factor for microbial keratitis. The ways in which the overnight OK lens-wearing modality may modulate this risk are unclear. In the event that it is demonstrated that overnight OK carries unacceptable risk compared with other contact lens modalities, the modality is doomed. In contrast, if the risks associated with overnight OK are found to fall within limits currently accepted in clinical contact lens practice, then OK may survive this particular challenge.

Permanency of corneal and refractive changes

The long-held dream of OK has been permanency of the lens-induced refractive change. Despite anecdotal reports of long-lasting effects with traditional OK, clinical studies dispelled this illusion and it was reluctantly accepted that the effects of OK on corneal curvature, refractive error and unaided vision are temporary and reversible. Periodic retainer lens wear is necessary to maintain the refractive change achieved by OK lens wear.

During the late 1990s, it was proposed that topical hyaluronidase and similar formulations could be used to loosen stromal collagen bonds prior to OK lens application, and then to 'reset' the stromal structure after successful corneal reshaping.[107] This technique was referred to as corneaplasty. I am unaware of any reports in the literature of corneal or refractive outcomes using this technique and this suggests that trials have not been promising. This is not surprising given our current understanding of the corneal response to OK, which primarily implicates thinning of the central epithelium and argues against significant stromal bending. Nevertheless, there is increasing evidence that the stroma plays a subtle but important

role in the corneal and refractive changes induced by OK lens wear. It is conceivable that a refinement of the concept of corneaplasty could be used to facilitate or optimise more permanent corneal reshaping in the future.

SUMMARY

This review is intended to provide an update on the current state of the art of overnight OK using reverse-geometry lens designs. I have summarised the history of traditional daily wear OK (1960s to 1980s) and the reasons for the recent resurgence in interest in the new modality of overnight OK using reverse-geometry lens designs (1990s to the present). It is clear that modern overnight OK is considerably more efficacious than traditional OK, as summarised in Tables 1 and 2, in terms of refractive error change and improvements in unaided vision. Onset of the effects of overnight OK lens wear is much more rapid than traditional OK, with most change occurring after the first night of lens wear and stability of refractive change after seven to 10 days. Mean reductions in myopic refractive error of between 1.75 and 3.33 D and individual reductions of up to 5.00 D have been reported, while most patients achieve 6/6 unaided vision or better. The induction of higher order aberrations, in particular spherical aberration, has been described and this may affect subjective vision under conditions of low contrast and pupil dilation. Patient satisfaction with overnight OK has been reported as similar to or better than other popular modalities of contact lens wear. Available evidence indicates that the corneal changes induced by overnight OK are fully reversible on cessation of lens wear.

The refractive effect in OK is achieved by central epithelial thinning and mid-peripheral epithelial and stromal thickening, without significant corneal bending. The nature of these tissue changes at a cellular level is actively under investigation, due to concerns about compromise of the epithelial barrier and the potential for increased risks of corneal infection. Indeed, an alarming number of case reports of microbial keratitis in this modality has been published since 2001. Analysis of these cases can provide some insight into the particular risk factors in overnight OK. However, there are insufficient data to comment on the absolute frequency of microbial keratitis in overnight OK or on the relative risks compared with other contact lens modalities.

Recent research on stromal contributions to the OK effect, particularly relating to overnight oedema, was also summarised in this article. Finally, emerging issues in orthokeratology, including myopic control, correction of other refractive errors and permanency of the OK effect are discussed. The future of overnight OK will depend on the resolution of current concerns about safety of the technique and the success of new applications of OK, particularly in terms of control of myopia and the correction of refractive errors such as astigmatism and hyperopia. Further developments of this exciting contact lens modality are awaited with interest.

ACKNOWLEDGEMENTS

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